UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,128	11/12/2003	Peter Gruber	225198	6230

23460 7590 08/20/2008

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER	
CARTER, KENDRA D	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
08/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,128	GRUBER, PETER	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7,9-16,23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-7,9-16,23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/21/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 21, 2008 has been entered.

The Examiner acknowledges the applicant's remarks and arguments of May 21, 2008 made to the office action filed December 21, 2007. Claims 1, 2, 4-7, 9-16, 23 and 25 are pending. Claims 1, 2, 9 and 25 are amended and claims 3, 8, 17-22 and 24 are cancelled.

In light of the amendments, all previous rejections are withdrawn.

Due to the amendment to the claims and all previous rejections being withdrawn, the new rejections are made below.

Applicant's arguments have been considered and are addressed below as they pertain to the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(1) Claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25 rejected under 35 U.S.C. 103(a) as being unpatentable over Wehling et al. (US 5,178,878) in view of Huber (US 4,122,157), and in further view of Battista (US 3,146,168).

Wehling et al. teach a solid pharmaceutical dosage form adapted for direct oral administration to a human comprising: a mixture of at least one saliva activated effervescent agent and a plurality of microparticles, each said microparticle including at least one systemically distributable pharmaceutical ingredient and a protective material substantially encompassing said pharmaceutical ingredient, wherein the dosage form being substantially completely disintegrable so as to release said microparticles upon exposure to saliva, said at least on effervescent agent being present in an amount which is effective to aid in rapid disintegration of said dosage form without chewing, and

thereby release said microparticles (see claim 1, addresses claims 1 and 25). The microparticle may incorporate a core incorporating a dispersion of the pharmaceutical ingredient in a first protective material and a coating of a second protective material, which may be the same as or different from the first protective material surrounding the core. Alternatively, a microparticle may incorporate a core consisting essentially of the pharmaceutical ingredient and a coating incorporating the protective material (see column 9, lines 52-60; addresses claims 1 and 25). The microparticles desirably are between about 75 and 600 microns (i.e. .075 and 6 mm) mean outside diameter (see column 9, lines 64-65; addresses claim 16). The effervescent tablets have a dissolution time of less than about 1.0 minutes when administered by mouth (see column 13, lines 11-12; addresses claim 1). The protective material may incorporate polymers such as those conventionally utilized in protective materials for microparticles such as gelatin, methylcellulose and carboxymethylcellulose (i.e. hydratable pharmaceutically acceptable polymer; see column 11, lines 38, 39, 49 and 52; addresses claims 1 and 25). The effervescent disintegration agent(s) include compounds which evolve gas upon exposure to saliva in the mouth (see column 5, lines 51-56). Such water activated materials are kept in a generally anhydrous state with little or no absorbed moisture (see column 5, lines 63-65; addresses claims 1 and 25). The acid source of the activated materials (i.e. salivation-promoting agent) include citric acid, tartaric acid, malic acid, fumaric acid and adipic acid (see column 5 lines 66-68 to column 6, lines 1-3; addresses claims 1, 8, 9 and 25). The effervescent sensation is not only pleasant to the patient but also tends to stimulate saliva production, thereby providing additional

water to aid in further effervescent action (i.e. salivation-promoting agent; see column 2, lines 52-55; addresses claim 1). Upon disintegration of the tablet, the microparticles are released and can be swallowed as a slurry or suspension of the microparticles (see column 2, lines 59-62; addresses claim 1). The dosage form will provide substantially prompt release of the pharmaceutical ingredient (see column 3, lines 21-24; addresses claim 15).

In regards to the limitation of claims 1 and 25, that upon the composition coming in contact with saliva it forms a "consistent, coherent, soft, moldable, viscous particle paste in which the particles are stuck together, which is slippery on the surface and does not adhere to the oral mucosa, and which prevents active ingredient-containing particles escaping from the particle paste, and release of active ingredient in the mouth", is considered an inherent property of the composition. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established. Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). The above also applies to the following limitation: promoting a flow of saliva which is sufficient to form said coherent, moldable, viscous particle pasts within less than 20 seconds of claim 1.

Wehling et al. does not teach the coating consisting of two or more layers as disclosed in claim 10, nor are the viscosity parameters of the hydratable polymer taught as disclosed in claims 2, 4, 10, 11 and 12.

Huber teaches a sustained release tablet of nitrofurantoin that can be in an effervescent tablet form (see tablet and column 2, last line). The *in vitro* rate of nitrofurantoin dissolution can be determined as a function of the viscosity of the hydroxypropyl methylcellulose employed. High viscosities of hydroxypropyl methylcellulose within the useful concentration range release the drug too slowly and result in diminished drug absorption and efficacy. Low viscosities of hydroxypropyl methylcellulose within the useful range result in too rapid a release of the drug causing an unacceptable incidence of nausea and anorexia in the patient. In order to obtain acceptable in vitro dissolution rates of from 33 to 66 mg of nitrofurantoin released during the first hour, the hydroxypropyl methylcellulose employed must have a viscosity of from 90 to 120 cps. Example 6 illustrates the critical nature of the viscosity of hydroxypropyl methylcellulose employed in obtaining the desired release rate of nitrofurantoin from the slow release portion of the tablet of the present invention (see column 4, lines 19-36). The preferred embodiment comprising a layered tablet comprising a rapid release layer and a slow release layer (see column 4, lines 37-40).

Battista teach that protective colloids increase smoothness of the material in the mouth or vary its texture. Suitable colloids include conventional gums like Arabic starches and starch derivatives, water-dispersible cellulose derivatives such as sodium carboxymethyl cellulose, and pectin (see column 8, lines 13-29).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the compositions of Wehling et al. and multiple layers and viscosities because of the following teachings: 1) Wehling et al. teaches that the microparticle may incorporate a core incorporating a dispersion of the pharmaceutical ingredient in a first protective material and a coating of a second protective material, which may be the same as or different from the first protective material surrounding the core (see column 9, lines 52-60; addresses claims 1 and 25); 2) Huber teaches that effervescent tablets can comprise layers to achieve different release characteristics (see column 4, lines 37-40); 3) Huber teaches that in vitro rate of nitrofurantoin dissolution can be determined as a function of the viscosity of the hydroxypropyl methylcellulose employed (see column 4, lines 19-36); and 4) although Huber does not teach the ionic polymers claimed in claim 1a, Battista et al. teaches that these polymers are all considered equivalent and that these polymers also have the property to increase smoothness of the material in the mouth or vary its texture. Thus, one would be motivated to adjust hydratable polymers such as those listed as an acceptable polymer in Applicant's claim 1a, and add layers to achieve a desirable release rate of the active drug.

(2) Claims 5 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wehling et al. (US 5,178,878) in view of Huber (US 4,122,157), and in further view of Battista (US 3,146,168) as applied to claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25 above, in further view of Kobayashi et al (US 5,476,668).

The teachings of Wehling et al., Huber, and Battista are as applied above to claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25.

Wehling et al., Huber, and Battista et al. do not specifically teach that the polymers have an average particle size not exceeding 200 microns, as recite in claim 5, or wherein the outermost layer has a polymer particle size not exceeding 50 microns, as recited in claim 13.

Kobayashi et al. teaches that cellulose ethers (e.g. hydroxypropyl methyl cellulose) are known to be used for film coating of pharmaceutical preparations (see column 1, lines 15-40, in particular.) Kobayashi et al. teaches that the cellulose ethers can be obtained having a high degree of polymerization, and thus a higher viscosity, than other low degree polymerization forms (see column 1, lines 15-40, in particular.) Kobayashi et al. teaches that the cellulose ethers with the high degree of polymerization

can be pulverized to an average particle size on the order of 50 microns, which meets the range limitations as recited in claims 5 and 13.

Accordingly, it is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to provide the cellulose ether particles having a high degree of polymerization as taught by Kobayashi et al. in the coated particle composition of Ibsen, because Wehling et al. in view of Huber teach that the coating can comprise polymers such as cellulose ethers, including hydroxypropyl methyl cellulose, and that such polymers can be selected in relation to their degree of polymerization to provide a desired viscosity, whereas Kobayashi et al. teaches a particulate form of cellulose ether particles having a high degree of polymerization and thus a high viscosity. Thus, one of ordinary skill in the art would have been motivated to provide the cellulose ether particles with the high degree of polymerization in the coated particle composition of Wehling et al. in view of Huber, with the expectation of providing polymer capable of providing a viscous medium about the particles upon contact with water (i.e. saliva).

(3) Claims 6 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wehling et al. (US 5,178,878) in view of Huber (US 4,122,157), and in further view of Battista (US 3,146,168) as applied to claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25 above, in further view of Alkire et al. (US 5,607,697)

The teachings of Wehling et al., Huber, and Battista are as applied above to claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25.

Wehling et al., Huber and Battista do not specifically teach wherein the coating is present in an amount of from 5 to 75% by weight, based on the essentially anhydrous composition (claim 6), or 0.25 to 50% by weight on the second outermost layer and 3 to 60% on the outermost layer as disclosed in claim 14.

Alkire et al. teach a taste masking microparticle oral dosage form (see title) comprising at least one saliva activating effervescent agent that dissolves in the mouth of a patient without chewing (see claim 2). The coating material is provided in an amount of at least about 5% by weight or from 5% and about 75% by weight of the microparticle (see claims 12 and 14). The upper limit of protective coating material used is generally less critical, except that where a rapid release of the active ingredient is desire, the amount of coating material should not be so great that the coating material impede the release profile of the active agent or pharmaceutical ingredient when ingested. Thus it may be possible to use greater than 100 percent of the weight of the core thus providing a relatively thick coating. Generally, however, no more than about 75 percent of the weight of the microparticle will be coating material and, more preferably, no more than about 50 percent of the weight of the microparticulate will be coating. Microparticles in accordance with the present invention may range in size (see column 7, lines 27-37).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Wehling et al. in view of Huber and the percentages of coating as disclosed in Applicant's claims 6 and 14 because both Alkire et al. and Wehling et al. teach compositions that dissolve in the mouth without chewing. Also, Alkire et al. teaches that the upper limit of protective coating material used is generally less critical, except that where a rapid release of the active ingredient is desire, the amount of coating material should not be so great that the coating material impede the release profile of the active agent or pharmaceutical ingredient when ingested (see column 7, lines 28-32). Thus, one skilled in the art would know to adjust the percentage of coating to obtain the desired release profile.

(4) Claims 7 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wehling et al. (US 5,178,878) in view of Huber (US 4,122,157), and in further view of Battista (US 3,146,168) as applied to claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25 above.

The teachings of Wehling et al., Huber, and Battista are as applied above to claims 1, 2, 4, 9, 10, 11, 12, 15, 16 and 25.

Wehling et al. does not specifically teach the specific active ingredients disclosed in claim 7, or a medical product pack comprising the composition of claim 1 and the

instructions that the composition be taken by direct administration into the mouth without liquid and without chewing as disclosed in claim 23.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Wehling et al. and the specific active ingredients disclosed in claim 7 because Wehling et al. teach that the pharmaceutical active agent may include without limitation antacids, analgesics, anti-inflammatories, antibiotics, laxatives, anorexics, antiasthmatics, antidiuretics, antidiuretics, antiflatuents, antimigraine agents, antispasmoidcs, sedatives, antihyperactives, tranquilizers, antihistamines, decongestants, betablockers, and combinations thereof (see column 4, lines 56-63). Thus, the many compounds disclosed in Applicant's claim 7 fall in the above class of compounds disclosed by Wehling et al.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Wehling et al. and the instructions that the composition be taken by direct administration into the mouth without liquid and without chewing as disclosed in claim 23 because Wehling et al. teach a composition comprising at least on effervescent agent being present in an amount which is effective to aid in rapid disintegration of said dosage form without chewing (see claim 1). Additionally, Wehling et al. teach that the effervescent system reduces the need to chew and protects the microparticles (see column 4, lines 6-7). Thus, one skilled in the art

would be motivated to provide instructions to not chew because it protects the microparticles and there is no need to chew the dosage form.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

> Applicant argues that Wehling does not disclose any water soluble organic acids or salts thereof as possible ingredients of the protective material. Furthermore, Wehling's protective material is not necessarily a coating on the microparticles; it may also serve as a mere matrix for the active agent. In Wehling's formulation the effervescent disintegrating agent is only mixed with the microparticles, not coated on the microparticles as stated in the amended claims. In regards to claims 1 and 25, the limitations of the properties of the composition should be afforded full patentable weight and not dismissed as an inherent property.

The Examiner disagrees because the organic acids are also salivation-promoting agents, in which are in the protective layer (see column 2, lines 52-55; and column 5, lines 51-68 to column 6, lines 1-3). Additionally, Wehling et al. teaches that the micropartilces may incorporate a core incorporating a dispersion of the pharmaceutical ingredient in a first protective material and a coating of a second protective material, which may be the same as or different from the first protective material surrounding the core. Alternatively, a microparticle may incorporate a core consisting essentially of the pharmaceutical ingredient and a coating incorporating the protective material (see

column 9, lines 52-60). Thus, the microparticles can be coated with a second protective material different from the microparticles.

In regards to the properties of the composition, the Examiner upholds the view that the composition coming in contact with saliva it forms a "consistent, coherent, soft, moldable, viscous particle paste in which the particles are stuck together, which is slippery on the surface and does not adhere to the oral mucosa, and which prevents active ingredient-containing particles escaping from the particle paste, and release of active ingredient in the mouth", is considered an inherent property of the composition. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established. Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). The above also applies to the following limitation: promoting a flow of saliva which is sufficient to form said coherent, moldable, viscous particle pasts within less than 20 seconds of claim 1.

> The Applicant argues that the Wehling's formulation contains an effervescent disintegration agent and thus largely disintegrates upon contact with saliva into individual microparticles, which does not teach the required form of particle paste. Additionally, Wehling states that the overall solubility of the food acids are less important, where as the amended claims mandate that the acid be water soluble. Lastly, a person skilled in the art would not provide Wehling's formulation with instructions that it be taken without chewing if that formulation was lacking the effervescent disintegration agent.

The Examiner disagrees because the effervescent tablet forms a slurry or suspension or the microparticles that are therefore easy to be swallowed (see column 2, lines 59-62). In regards to the acid, Wehling teaches the claimed acids, therefore a "water-soluble organic acid" is taught as claimed in claim 1. In regards to the instructions, the Examiner upholds the argument that this limitation is taught by Wehling because Wehling et al. teach a composition comprising at least on effervescent agent being present in an amount which is effective to aid in rapid disintegration of said dosage form without chewing (see claim 1). Additionally, Wehling et al. teach that the effervescent system reduces the need to chew and protects the microparticles (see column 4, lines 6-7). Thus, one skilled in the art would be motivated to provide instructions to not chew because it protects the microparticles and there is no need to chew the dosage form.

> The Applicant further argues that Huber has a release rate within the first hour, whereas Wehling prefers a much faster release of within the first 30 minutes. Thus, one skilled in the art would not employ these hydroxypropylmethyl celluloses as a protective material.

The Examiner disagrees because Huber is used to give and example that dissolution can be determined as a function of the viscosity of the hydroxypropyl methylcellulose employed. Thus, one skilled in the art can choose these types of polymers and adjust their viscosity to obtain the desired dissolution rate.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/K. D. C./
Examiner, Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617